IDENTIFYING THE QUALITY OF THE CELL IMAGES ACQUIRED WITH DIGITAL HOLOGRAPHIC MICROSCOPY USING CONVOLUTIONAL NEURAL NETWORKS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application is a national phase filing under 35 U.S.C. § 371 of International Patent Application No. PCT/EP2018/068345, filed Jul. 6, 2018, which is incorporated herein by reference in its entirety. This application claims the benefit of U.S. Provisional Application Ser. No. 62/545,517 filed Aug. 15, 2017, which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

[0002] The present disclosure relates generally to using convolutional neural networks (CNN) to identify the quality of image acquired using digital holographic microscopy (DHM) and other microscopy techniques. The various systems, methods, and apparatuses described herein may be applied to, for example, enhance classification workflows and the subsequent diagnosis decisions by removing out of focus or poor quality images from analysis.

BACKGROUND

[0003] Digital holographic microscopy (DHM), also known as interference phase microscopy, is an imaging technology that provides the ability to quantitatively track sub-nanometric optical thickness changes in transparent specimens. Unlike traditional digital microscopy, in which only intensity (amplitude) information about a specimen is captured, DHM captures both phase and intensity. The phase information, captured as a hologram, can be used to reconstruct extended morphological information (such as depth and surface characteristics) about the specimen using a computer algorithm. Modern DHM implementations offer several additional benefits, such as fast scanning/data acquisition speed, low noise, high resolution and the potential for label-free sample acquisition.

[0004] DHM is particularly well suited for acquiring images of blood cells for classification purposes, or to perform subsequent diagnosis decisions. For example, one of the important features of a complete blood count is to classify the white blood cells (WBC) into five different categories as the imbalance of the number of cells in one or more category helps in disease diagnosis. Automatic classification of the WBC can be performed by applying advanced image analysis techniques on the cell images acquired using DHM. The quality of the cell image is crucial and would affect the accuracy of the classification. Therefore, it is important to be able to identify good quality cell images.

[0005] Off-axis holographic microcopy system creates holograms where there is a modulating pattern over the entire field of view due to a small angle between object and reference beam. Furthermore, as depicted in the specific DHM set up shown in FIG. **1**, the reference beam is created from the object beam using two lenses and a pinhole to erase the object spatial signature and to provide a uniform plane waves for creating an interference or hologram image. The focal length would greatly affect the quality of the acquired cell images. The distance between the focal plane and the object impacts the appearance of the phase images and their quality. FIG. **2** illustrates example cell images with different quality. In the top row, the cells are in focus and the information content of the image can be used to discriminate among the different cell types. The images in the bottom row are of cells that are out of focus and distorted. The image quality is very poor and cannot be used in a diagnosis workflow.

SUMMARY

[0006] Embodiments of the present invention address and overcome one or more of the above shortcomings and drawbacks, by providing methods, systems, and apparatuses related to identifying the quality of the cell images acquired with a microscopy device using a convolutional neural network (CNN). Briefly, a CNN is trained to determine whether cells are in focus or out of focus in an acquired image. In some embodiments, based on this determination, instructions may be provided to the microscopy device to adjust the focal length so as to bring the acquired images into focus.

[0007] According to some embodiments, a computer-implemented method for detecting out of focus microscopy images includes acquiring microscopy images depicting cells, and extracting one or more sets of pixels from the microscopy images. Each set of pixels corresponds to an independent cell. One of a plurality of image quality labels are assigned to each set of pixels indicating the degree to which the independent cell is in focus. A classifier is trained to classify the set of pixels into the image quality labels. The classifier is configured according to a multi-layer architecture and the training results in determination of weights for connecting layers in the multi-layer architecture. A deployment of the classifier is created based on the multi-layer architecture, the weights, and the image quality labels.

[0008] According to other embodiments, a computer-implemented method for performing adaptive focusing of a microscopy device includes acquiring a plurality of microscopy images depicting cells using a microscopy device, and extracting one or more sets of pixels from the microscopy images. Each set of pixels corresponds to an independent cell. Then, a trained classifier is used to assign one of a plurality of image quality labels to each set of pixels indicating the degree to which the independent cell is in focus. If the image quality labels corresponding to the sets of pixels indicate that the cells are out of focus, a focal length adjustment for adjusting focus of the microscopy device is determined using a trained machine learning model. Then, executable instructions are sent to the microscopy device to perform the focal length adjustment.

[0009] According to other embodiments, a system for performing adaptive focusing of a microscopy device comprises a microscopy device configured to acquire microscopy images depicting cells and one or more processors executing instructions for performing a method that includes extracting pixels from the microscopy images. Each set of pixels corresponds to an independent cell. A trained classifier is used to assign one of a plurality of image quality labels to each set of pixels indicating the degree to which the independent cell is in focus. If the image quality labels corresponding to the sets of pixels indicate that the cells are out of focus, a focal length adjustment for adjusting focus of the microscopy device is determined using a trained